PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 4 : G01N 15/12, 35/00

A1

(11) International Publication Number: WO 87/ 00280

(43) International Publication Date: 15 January 1987 (15.01.87)

(21) International Application Number: PCT/US86/01350

(22) International Filing Date: 24 June 1986 (24.06.86)

(31) Priority Application Number: 748,003

(32) Priority Date: 24 June 1985 (24.06.85)

(33) Priority Country: US

(71) Applicant: CELLTRAK DIAGNOSTIC SYSTEMS, INC. [US/US]; 30 Lindeman Drive, Trumbull, CT 06611 (US).

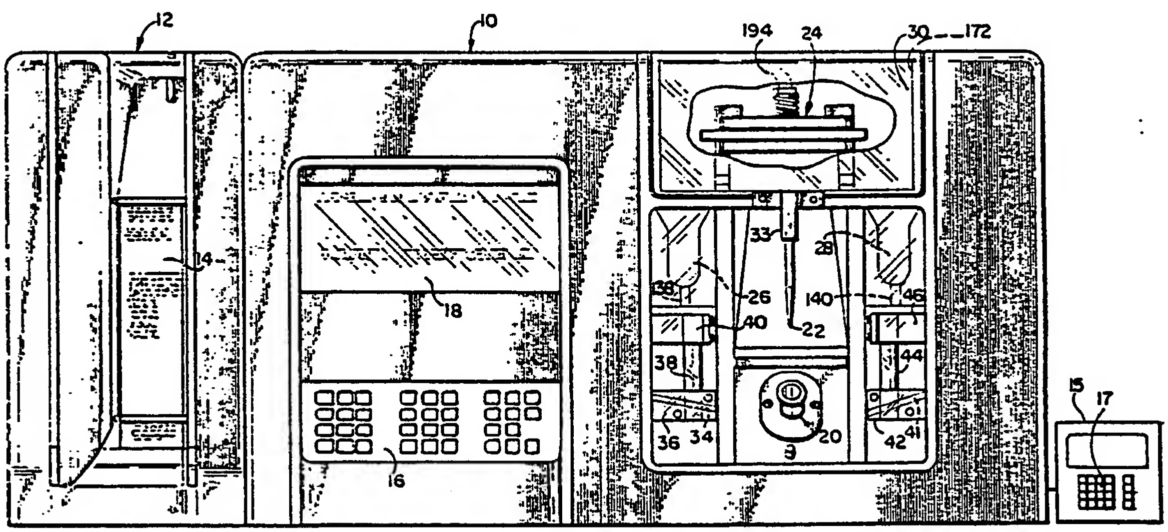
(72) Inventors: HENNESSY, James, W. ; 31 Overlook Place, Trumbull, CT 06611 (US). ANGEL, Henry, R. ; 706 Burr Street, Fairfield, CT 06430 (US). CARLSON, Richard, A. ; 435 Yale Avenue, Meriden, CT 06450 (US).

(74) Agent: DORFMAN, John, C.; Dann, Dorfman, Herrell and Skillman, 1310 The Fidelity Building, 123 South Broad Street, Philadelphia, PA 19109 (US).

(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent).

Published
With international search report.
With amended claims.

(54) Title: CONTROL MEANS FOR A BLOOD ANALYSIS SYSTEM



(57) Abstract

A blood count analysis apparatus includes a receptable (20) for receiving a blood sample container, an aspirator (22) for aspirating sample to be conveyed to and through a multi-position slide valve (24). Red blood count container (26) and white blood count container (28) receive properly diluted samples. Diluted samples from the red blood count container (26) are fed by a tubular portion of the container to a counting section (34, 36, 38, 40). Diluted and lysed white blood cells from the white blood cell count container (28) are counted in count section (40, 42, 44). Aspiration, valve movement and counting are controlled by a microprocessor (250). The apparatus also includes a keyboard (16) and a plug-in differential keyboard (17) to provide the input information for the blood test to be performed.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GA	Gabon	MR	Mauritania
AU	Australia	GB	United Kingdom	MW	Malawi
BB	Barbados	HU	Hungary	NL	Netherlands
BE	Belgium	IT	Italy	NO	Norway
BG	Bulgaria	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	LI	Liechtenstein	SN	Senegal
CH	Switzerland	LK	Sri Lanka	SU	Soviet Union
CM	Cameroon	LU	Luxembourg	TD	Chad
DE	Germany, Federal Republic of	MC	Monaco	TG	Togo
DK	Denmark	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali		
FR	France				

CONTROL MEANS FOR A BLOOD ANALYSIS SYSTEM

Field of the Invention

The present invention relates to a system and subsystems for controlling an instrument for automatically analyzing blood. The system includes means for calibrating the instrument, controlling the sequence and operation of its parts and automatically displaying instructions in connection with the controlling of the system and test results. More specifically, the present invention relates to means for computer control of calibration, operation and related functions of a hematology system such as that taught in U.S. patent application Serial No. 675,378, filed November 27, 1984, and assigned to Angel Engineering Corporation, the assignee of the present invention.

Background of the Invention

What is known about the prior art has more to do with the structure described in application Serial No. 675,378 and, therefore, has been stated in that application. The present invention relating to control functions and computer control applies to the field more broadly than merely use in the system or apparatus of application Serial No. 675,378. It is believed to provide some completely new approaches in the blood analysis field.

Summary of the Invention

The aforesaid hematology system of U.S.patent application Serial No. 675,378 permits automatic handling of most blood tests. This system provides the

apparatus for accomplishing blood analysis and the specification describes how the apparatus functions. The present invention relates to the computer control which was not specifically described or shown but the possibility of whose presence could be inferred through the input and output apparatus of the total instrument disclosed.

The present invention relates to a computer controlled system which may employ a microprocessor of known type which functions to control the various operational functions and sequences of the apparatus. For example, it controls the aspiration and the discharge of diluent into the system. It controls the positioning of the movable valve, which is preferably a multi-position rotary valve, into the precise operating positions required for each of the operational steps of any test. The computer also controls cleaning of the passages of the movable valve, cleaning the vacutainer input chamber and the aspirator tip compartment and such other maintenance functions as may be required. The movable valve may also have its parts manually or automatically separated for manual cleaning as described in application Serial No. 675,378.

The system also sees to calibration and the numerical accuracy in calibration. It is provided with security in the form of an access code. The system permits changes both of the security access code and of calibration, in both cases either at the system or from a remote location, and it provides an automatic remote station inquiry technique for obtaining information

from the manufacturer for properly performing various tests. After the tests have been performed, it calculates various parameters needed for output. It outputs them on a display and issues a printed ticket showing the results of the test.

The hematology system of the present invention provides a system capable of quantitative determination of the following: a white blood cell count (WBC); a red blood cell count (RBC); hemoglobin (HGB); mean corpuscular volume (MCV); platelet count (PLT); and mean platelet volume (MPV). The system is also capable of calculating from test results of the RBC, HGB, MCV, PLT and MPV the following: hematocrit (HCT); mean corpuscular hemoglobin (MCH); mean corpuscular hemoglobin concentration (MCHC); and thrombocrit (TCT).

Description of a Preferred Embodiment of the Invention

For a better understanding of the present invention, reference is made to the accompanying drawings in which:

Fig. 1 is an elevational view from the front of a proposed apparatus in accordance with the present invention;

Fig. 2 is a schematic diagram showing the flow and control of fluids through the device;

Figs. 3a, 3b, 3c and 3d are sequential schematic views intended to show fluid flow paths through the rotary valve in successive positions;

Fig. 4 is a block diagram showing schematically the broad interrelationships of components affected by

or affecting the computer;

Fig. 5 is a representation of keyboard layout of the keyboard shown in Fig. 1;

Fig. 6 is a block diagram showing schematically drive motor controls for motor driven parts of the system;

Fig. 7 is a plot of stepper motor speed versus time;

Figs. 8a, 8b and 8c are plots showing distribution of platelets in a test sample by size, the platelet count versus the logarithm of particle size and the step change of the logarithm scale versus the logarithm of particle size;

Fig. 9 is a typical print out by the printer of the present invention; and

Fig. 10 is a block diagram of an analog circuit for modifying various blood constituent related information.

The hematology system of the present invention provides controls for apparatus described in U.S. application Serial No. 675,378, providing an automated microprocessor based benchtop, multiparameter hematology instrument. The system consists of the analyzer or microprocessor, a printer, a differential counter, supplies various reagents and consumables and the fluid system for automatically handling the blood samples. The complete system requires a total work area of approximately four feet by two feet.

The throughput of the system is approximately 60 specimens per hour. The displays and indicators on the

screen output will provide the operator with information concerning the status of every test and will aid the operator in normal operation, or calibration, or will prompt to alert the operator to troubleshoot problems such as clogs and overrange. The modular construction makes for easy servicing.

Referring first to Fig. 1, there is illustrated a preferred blood analysis apparatus in accordance with the present invention, housed within two adjacent housings 10 and 12. Housing 10 encloses and supports the mechanical and fluid handling portions of the system as well as input control and display functions. Add on cabinet 12 houses a printer responsive to data generated by the computer within cabinet 10 to print out on slips 14 a hard copy of the blood test results. Input information, such as the nature of a blood test required, is input to the system through keyboard 16 to the internal computer and electronic system. To make some white blood counts, a cytologist making a visual count may need a differential input 15 to manually introduce counts as they are made. A module with a plug-in connection through housing 10, may be added permitting input from differential keyboard 17. Although not suggested by the drawing, the connecting cord should be sufficiently long to permit movement from place to place, such as to microscope and desk locations. Output of test information is displayed on alpha numeric display 18, and may be printed out on slips 14 if the printer in housing 12 is employed.

Blood samples may be handled automatically either with open or sealed vacuum containers. Vacuum containers are inserted into receptacle 20 with their resilient closure down for automatic puncture and

removal of blood samples. Samples from open containers are fed into the system through aspirator 22. The system has at its heart a rotary valve 24 which is repositioned for various steps in the automatic handling of the blood sample including a dilution step by which blood properly diluted for a red blood count is placed into container 26. A properly diluted sample for a white blood count is placed in container 28. These containers are open and accessible from above when the hinged transparent cover 30 conforming to the shape of the front and top of the housing is open. Cover 30 rotates about a hinge at its top edge to expose valve 24 for maintenance and repairs. Raising cover 30 also allows hand diluted samples to be added to the containers 26 and 28 from above.

A start switch lever 33 is also provided just below the cover. The start switch is actuated to enable the system to begin its sequence of test steps.

Properly diluted red blood samples are fed by suitable tubular connection from container 26 to the counter portion. The counter container consists of a passage 34 in block 36 generally tangent to a jewel orifice of great precision in the sidewall of vertically oriented tube 38. Tube 38, in turn, is supported by a bracket 40. Similarly, white blood counts are made by passing the diluted and lysed white blood sample from container 28 by suitable tubing connection through passage 140 into block 42 so that it passes tangent to tube 44 whose sidewall contains a jewel orifice of suitably different dimensions. Tube 44 and support block 42 are supported on the housing by

bracket 46.

It will be appreciated that internally of the housing 10 there are located a great many necessary fluid system components which are considered in connection with Fig. 2 and lines as well as the computer, counter, processing means, input circuitry, and the like, which are generally considered in connection with Fig. 4 and which, while conventional as components, are provided in a new combination to provide an automatic, or semi automatic, computer controlled blood test apparatus.

The principle parts of the fluid system are shown schematically in Fig. 2. Fig. 2 contains components, or parts related to the components already disclosed, as well as such additional components as are needed to complete the fluid system. It will be understood that the single lines shown, are intended to represent tubing or pipe which, in some cases, is flexible. No effort has been made, nor needs to be made, to explain conventional connections between such tubing or pipe and various components.

Input into the system is preferably through the aspirator tip 22 which draws blood from a container which is open, or, from a vacuum container inserted into the vacuum container input structure 20. In either case, input is through a multi-position slide valve, preferably a rotary valve 24, whose positioning is determined by what stage of the process is involved. In this connection, it should be noted that the lines shown as input to the rotary valve in Fig. 2 are,

indeed, merely input lines and their positioning relative to the valve in this schematic showing is not significant except that they are properly shown at the top or the bottom of the valve. Diluent is supplied from diluent supply 48 through valve 24 for various purposes including the filling of the 10 milliliter and 25 milliliter syringes 50 and 52, respectively. Diluted red blood test samples are collected and mixed in red blood count container 26 and white blood count test samples are collected and mixed in white blood count container 28. Lyse material for the processing of the white blood count is obtained from container 54.

A vacuum pump 56 provides a vacuum for various purposes including to reduce the pressure within internal waste container 58. It will be observed that the vacuum level is sensed by a vacuum sensor 64 which trips an alarm indicator such as a light or buzzer, indicating a problem relating to insufficient vacuum, if the pressure of the vacuum falls to a predetermined level. The vacuum sensor 64 also provides an output to the microprocessor proportional to the vacuum which is compared to a predetermined level by the microprocessor. The microprocessor then controls pump operation as required through buffer 62 to maintain appropriate vacuum level. Where very accurate vacuum level control is needed, vacuum regulator 60 is connected to the system to help smooth out variations that would otherwise occur in vacuum levels. Valve V18 to regulator 60 is closed when valves V6a and V6b are

opened and V4 is closed to apply pressure to the waste fluid tank 58 to clean it out through valve V6a to waste. At that same time, valve V8 is opened to atmosphere (ATM).

The receptacle 20 receives vacutainers so that they introduce blood into the system. A drain tube is located in the lowest portion of the tubular sidewall to provide a drain into the evacuation tube. The drain tube is connected to a vacuum source at an appropriate time in the sequence determined by the program controller function of the computer.

Pivotally supported on the sidewall of the cup support means, just below the guide tube, is a closure flap preferably spring loaded into a position closing the opening. This closure is pushed aside as the vacutainer is inserted. Separate sensor means detect when a vacutainer is inserted and when removed. The signals from the sensor means may be used to signal the program means to activate the rotary valve 24 to the proper position for receiving a blood sample from the vacutainer and for enabling syringe movement drawing blood from the container.

Similarly, when the vacutainer is withdrawn at the end of the processing, its removal is sensed. The sensory signal, in turn, may enable an adjustment of the rotary valve and a reverse flush with the diluent from the syringe 50. This flush will clean out the blood from the hypodermic needle. The stream of diluent will be deflected by the closed flap, captured in the gutter and evacuated by evacuation tube.

Considering now the aspirator structure, the aspirator tip 22 is supported on the housing and connected by tubing to the rotary valve 24 as schematically shown in Fig. 2. The aspirator tip 22 is supported to protrude downwardly and out of an alcove. The aspirator is thus positioned so that a beaker or other blood containing vessel can be held under it. A cover is provided with spring means which tends to move the cover into closed position. The cover supports an enclosure in the form of a portion of truncated cone enclosing the aspirator tip 22 in the closed position of the cover. The cover is open to enable placement of a blood sample container under the aspirator tip. When the container is removed, the cover can be manually returned about its pivot means to its closed position. Sensor means detect a closed condition of the cover to activate the rotary valve to a position to provide cleaning fluid to the aspirator tip 22. After the container is removed, and presumably the outside of the aspirator tip wiped clean, the closure can be moved by the handle to closed position wherein diluent from syringe 50 is forced through the aspirator to clean it. The tip enclosure provides a liquid collecting basin which directs the cleansing solution into a drain.

As seen in Fig. 1, on the opposite sides of the intake are the red blood cell receptacle 26 and the white blood cell receptacle 28. These containers in the system are designed to be filled automatically and simultaneously. It is possible, however, for containers 26 and/or 28 to be filled manually with

properly diluted solutions of a given sample and tests performed on those solutions. Instead of processing the whole series of tests manually or automatically, the processing may be limited to partial or full test for either or both the red or the white cells. Alternatively, the system in some embodiments can take a manual dilution for a white cell count, and automatically draw off and perform the further dilution for a red blood count depending on its program capabilities.

Whether filled automatically or manually, the blood collected in containers 26 or 28 is then processed through passage of 138 or 140 in the bottom of the container. Advantageously, containers 26 and 28 are formed in clear, transparent blocks through which passage 138 and 140 are bored. Passage 138 is, in turn, connected to a tubular passage 34 in block 36 by means of a hose which connects conveniently to coupling 142 in the block. Similarly, passage 140 connects to a similar hose connection to passage 41 in block 42. Passage 34 is arranged to pass tangentially by the jewel orifice 146 (Fig. 2) pressed into the tube 38. Orifice 146 is schematically represented in Fig. 2 and an orifice 148 for the white blood cell processing is similarly represented in Fig. 2. On opposite sides of the orifice 146 are electrodes used in the pulse counting technique conventionally used in blood counting apparatus and broadly described, for example, in United States patent No. 3,921,066 of Angel Engineering Corporation. Specifically in each passage

34 and 41, there is provided an electrode which is placed along the periphery of the bore and connected by suitable electrical connection to a source of potential and the counting circuit. Inside tube 38 of insulating material is a larger electrode connected by a suitable electrical lead into the counting circuit.

It will be understood that the white blood cell count structure employing insulating tube 44 surrounded by block 42 containing passage 41 is similar to the red blood cell count structure except that orifice size is different and appropriate to the cells being counted.

Now considering the rotary valve 24 seen in Fig. 1, and schematically in Fig. 2, it will be appreciated that the valve is composed of three cylindrical blocks 162, 164 and 166, sometimes called discs, with the middle block or disc 164 rotatable about the spindle 168. It will be understood that each of the discs has ports through it. The ports in discs 162 and 166 are located in positions essentially corresponding to one another. Thus, they are axially aligned at all times. However, the ports in movable disc 164 are moved from one position to another in order to effect different combinations of connections as illustrated in Figs. 3a, 3b, 3c and 3d to be discussed hereafter.

Preferably, the spindle of the rotational valve is a tube provided with a hose 194 (Fig. 1) connecting it to a supply of cleaning solution to clean the surfaces between the discs. Means is provided to separate the discs and ports are provided in position to line up with the spacing between discs 164 and 166 and with the

spacing between discs 162 and 164, respectively, in the open position. While cleaning may be done manually and step by step as described in application Serial No. 675,378, the means provided may be automatic and thus under command of a processing program.

The upper and the lower discs 162 and 166 are provided with similar ports. Disc 162 has ports labeled A through H. Similarly, disc 166 has ports A' through H' in the same relative positions so that as aligned by key post 163, correspondingly lettered ports of disc 166 will be axially aligned with those of disc 162. The middle movable disc 164, however, has a different pattern of ports J through M which cooperate with the aligned ports in the other discs to perform different functions in the different positions of disc 164. In general, and contrary to the suggestion of the schematic line drawings of Fig. 3, in practice, the ports in the middle disc have been somewhat smaller in diameter than those in the outer discs. Additionally, each of the discs has double ports D, J and D', which, at least in one situation (Fig. 3b), are aligned. The two ports in disc 164 are together called J, but the smaller of the two is the port which performs the blood sample measuring function for red blood cell analysis, and only that smaller port is filled with blood sample. Both the smaller port of double port J and the single white cell test port K are intended for measurements of highly repeatable volumes.

The ports J and K need not be precision formed since they may be calibrated in the equipment, but they

must be stable in volume and not be subject to change in the normal use of the valve. The larger single hole is used in the white blood cell count since the amount of dilution required in the white blood count is relatively smaller than in the red blood count. In connection with the red blood count, the smaller of the pair of holes marked J is the one which is filled with the sample. In order to provide the selected amount of diluent required for the red blood count in a reasonable period of time, the larger parallel hole is provided and diluent is fed in parallel through both holes. Thereby, while the sample is being washed out of the small hole by some of the diluent, an additional greater volume of diluent will pass through the larger hole. The parallel paths enable enough diluent to pass through the valve 24 in the limited test time allowed for that valve position.

The various indexed valve positions assumed in operation have been shown highly diagramatically in Figs. 3a, 3b, 3c and 3d. It will be understood that in these diagrams, only those lines connecting the operative ports in a given position have been shown for clarity.

Fig. 3a shows the rotary valve position in which aspiration is occurring and the metering holes K and the smaller of the pair J, are filled in series. This is accomplished by connecting the aspirator tip 22 in series through ports A, J, A', B', K, B and into the syringe 50 as the plunger of that syringe 50 is withdrawn to draw the blood sample toward it.

Fig. 3b shows the valve position for dilution wherein the larger syringe 52 filled with diluent is emptied through both of the ports J in parallel, the smaller port containing the blood and the larger port without blood. The double ports J are in series with the corresponding double ports D and D' in discs 162 and 166. Referring to Fig. 2, the larger syringe 52 empties through the double ports, including the smaller port containing the small measured blood sample into the red blood count container 26. At the same time, the smaller syringe 50 empties through the port K filled with a larger measured quantity of blood, entering through port E and exiting port E' to place the mixture in the white blood cell count container 28.

Fig. 3c shows the rotary valve position in which the syringes 50 and 52 are charged from the diluent supply 48. This is done bringing a line through ports F, L and F' to syringe 50 and through ports C, M and C' to syringe 52.

Fig. 3d is the alternative position to the valve for aspirating blood from a vacutainer source. As in Fig. 3a, only the smaller of the J ports in disc 164 is filled in series with the larger K port in disc 164 by drawing fluid into syringe 50. This occurs in series through port G, smaller port J, port G', then, back through port H', red cell metering port K and port H to syringe 50.

While the valve 24 herein has been shown and described as a particular type of rotary valve, it will be clear to those skilled in the art that many changes

can be made in the rotary valve as shown or that a linearly sliding valve or other equivalent can be substituted for the purpose of this invention.

Referring now to Fig. 2, the overall operation of the fluid system will now be described. As will be described, the apparatus described thus far, plus other devices and mechanisms shown schematically in Fig. 2, are automatically controlled by the microprocessor computer system illustrated in Fig. 4. Sensed signals detecting key parts of the process are fed to the microprocessor to initiate, terminate or otherwise cue action provided by the program for automatic operation of the system. The microprocessor is contained within housing 10 using the input controls 16, seen in Fig. 1.

To begin the process, diluent is drawn from supply 48 by opening solenoid valve V17. In order to know the amount of diluent drawn into or dispensed, sensors 234 and 236 are mounted on the housing of the syringes 50 and 52, respectively, in each case to determine a "home" reference position and to enable digital counting of predetermined volume units of diluent drawn into or dispensed from the syringe in response to controlled rotation of a drive motor. After positioning rotary valve in the position shown in Fig. 3c, diluent fluid is then drawn into the syringes to essentially fill them. As a practical matter, the syringes are motor driven. Drive is preferably done positively, such as by providing a lead screw along the plunger handle of each syringe. A drive nut 238 may be

driven in either direction by motor 240 to move the plunger of syringe 50 upon command. A drive nut 242 is similarly driven by motor 244 to move the plunger of larger syringe 52. In each case, the motor may be provided with a hollow shaft sufficiently large to allow the lead screw to pass through the shaft along the axis of its motor with the drive nut affixed axially to the shaft.

With diluent in the syringes, the apparatus is ready to work and a blood sample may be drawn through the aspirator tip 22 from an open container by repositioning the rotary valve 24 to the position of Fig. 3a or from a vacuum container by repositioning the rotary valve to the position of Fig. 3d upon inserting the vacutainer into receptacle 20. In order to aspirate, vacuum is drawn by further withdrawal of the plunger of syringe 50, as illustrated in Figs. 3a or 3d. Either way, a sample is drawn into the smaller measuring bore of the pair of bores J and the large measuring bore K in disc 164. The sample is retained within those bores as the disc 164 is rotated to the position of Fig. 3b. A measured amount of diluent from syringe 50 is fed through bore K to wash out the measured volume of blood sample in the larger hole into the white blood count container 28 and provide sufficient diluent for the white blood cell test. At the same time, the measured proper amount of diluent from syringe 52 is fed through both of the two bores J to wash out the measured volume of blood sample therein and mix it with the proper amount of diluent in the red

blood count container 26. At this point, the normally closed valve V14 is opened for a very short measured time, on the order of one and a half second, to add the required amount of lyse from container 54 to dissolve red cells and release their contained hemoglobin. This occurs under pressure applied from pump 56.

Valves V3 and V9 which, like many of the valves of the system, are preferably pinch valve members located to pinch flexible hose portions of the line along which they are interposed. Opening normally closed valve V3 draws red blood count mixture into tube 34 past jewel orifice 146 due to the presence of a vacuum in an internal waste tank 58. Similarly, opening normally closed valve V9 draws white blood count mixture from container 28 through the tube 40 past jewel orifice 148 due to the presence of the vacuum in internal waste chamber 58.

After samples have been moved into the lines respectively passing jewel orifice 146 and 148 by opening valves V3 and V9, valve V5 is then opened briefly to interject an air bubble from 218 and 220 into each of the lines 138' and 140' from each of the red and white blood counting chambers 26 and 28. This opening is for a very short period, just long enough for air from pump 56 to form a discontinuity in the diluted blood sample. Valves V3 and V9 are then closed and valves V11 and V12 are opened to draw the respective blood samples through jewel orifices 146 and 148, respectively, due to the vacuum in the internal waste tank 58. The bubble interposed in the line forms

a visible, or otherwise sensible, discontinuity, which may be sensed as it passes a sensor along or in the line. Passage of the bubble between two sensing points along lines 138' or 140' represents the passage of an equivalent volume of the blood sample through the orifice to fluid volume contained in that line between the sensing points. Transparent tubing 138' may be employed between the red blood container 26 and the jewel 146, and similar transparent tubing 140' between white blood container 128 and jewel 148.

Such photosensors as seen in Fig. 2 are placed at the beginning and end of a measured length of the respective lines 138' and 140'. Discontinuities in the lines are sensed to respectively start and terminate the count of the counter, thus, applying the count to a known measured volume in each case. Sensors 222 along line 138' initiate such counting for the red blood count, and sensors 224 along line 140' initiate the counting for the white blood count. Sensors 226 along line 138' terminate the red blood count and sensors 228 along line 140' terminate the white blood count.

An HGB measurement is made while the sample is still in the white blood container 28 using the light source 230, and the HGB detector (photodiode) 230b.

Also, just before counting begins on the red blood count side, valve V17 is opened together with valve V15 and valve V11 to waste 58 to supply diluent, which is advantageously also an electrolyte solution, at a high rate to prime and fill from the back or internal side

of jewel orifice 146. During counting, valve V15 is closed but valve V13 is opened to cause a reduced flow of cleaning diluent through choke 232 past jewel orifice 146 to sweep away red blood cells to avoid recounting of those particles which otherwise might produce error due to their swirl around electrode 152 in tube 38.

Once the count is completed, the sample can be fully evacuated from the container 26 and 28 by opening valves V3 and V9.

The rotary valve 24 is then placed in the position of Fig. 3b, and clean diluent is passed through the measuring orifices and into the red and white blood count containers 26 and 28 to rinse them. Then, containers 26 and 28 are evacuated through valves V3 and V9 to internal waste 58.

The system can be designed so that the tubes normally containing fluid are kept wet by arranging the timing of evacuation to occur just before the new sample is introduced.

The system of the present invention makes possible completely automatic cycling which is programmed for computer control. Such programming enabling complete automation and rapid throughput through the device is made possible not only by the described features of the present invention but by the control system which will now be described.

The processes described are controlled by a microprocessor and associated system as shown in Fig. 4. The microprocessor 250 is provided with a keyboard input 16, as seen in Fig. 1 and in greater detail in Fig. 5, and may be supplied with a differential keyboard input 17 as well. Alternative outputs may be provided by way of display device 18 which may be a cathode ray tube or other type of alpha numeric display and optionally by a printer 252 which prints hard copy 14 as illustrated in Fig. 1. One of the major functions of the microprocessor is to provide programmed control of the steps of operation as described in connection with Fig. 2. There may be many kinds of controls involved, and these are lumped together and represented as a single box 254 labeled multiple system controls, most of which have feedback to the microprocessor of some sort, either from the controls or from means monitoring the device operated by the controls. In addition, there is a system calibration system 256 which, in this representation, also includes a security system (not separately represented). Additionally, there are system alarms 258, which, in some cases, may be local and self-operating and, in other cases, feed through the microprocessor to generate a message on the display and may actually be fed back out to some sort of annunciator system.

Particularly, the calibration and the security systems require memory 260, and other aspects of the system controls may require instructional memory as

well. Memory here is represented as a simple in/out representation but could take the form of one or more types of memory for the various memory functions.

In order to make the microprocessor responsive to input from a remote processor or input terminal 262, a modem 264 is ordinarily provided enabling transmission of messages over telephone lines by microwave or otherwise, as is widely known and understood in the art. Alternatively, other system matching communication links 266 such as RS-232 may be used or two or more systems may be used in parallel or to different remote locations.

A computer interface option is possible. Messages can be transmitted to a computer automatically at the end of a test or by operator command. A preferred interface is capable of bidirectional transfers.

The printer 252 is also an option which may not be needed by every user. The printer will provide a hardcopy fanfold or single ticket with the date, time, patient identification number with the corresponding data including the platelet histogram.

Referring to Fig. 5, the keyboard includes a panel 266 of numeric touch keys, which might also include control panels 268 and 270 providing keys to control various system function as suggested by legends on the keys. Some of the functions may alternatively be automatically controlled by the system in accordance with a preset program in memory, as well as being manually accessed and initiated through the input selection keys.

A differential count keyboard option is also available using plug in module 15 seen in Fig. 1. The differential keyboard 17 will enable the operator to enter the differential count. If CBC data is present in the system, it will be matched by I.D. number and printed automatically when the differential is run. The differential may also be printed without running a sample on the instrument by entering the appropriate I.D. number and manually selecting print. All data present under this I.D. number will then be printed. If the WBC count is available, the differential counter will print the absolute white counts as well as the data and differential.

Part of the multiple system controls involves a so-called intelligent controller 254'. Intelligent controller 254' as seen in Fig. 6 effectively controls the stepping motors 240 and 244 driving the syringes 50 and 52, respectively, and the stepping motor 182 driving the movable disc 164 of rotary valve 24. In accordance with the present invention, not only is the program for moving the syringes provided to accomplish each of the steps in the preset cycle but positioning is sensed and fed back to the intelligent controller so that the motor may be placed at a "home" position at least once each cycle. Thus, the stepping motor moves stepwise from one programmed position to another, its stopping point being determined by the direction and number of pulses fed to the stepping motor to drive the syringe or the rotary valve from one predetermined position to another.

Considering syringe 50 for example, the fluid in the syringe may be monitored by a sensor 234 receiving light from a light source 233 so that when the plunger occludes the light, a step or pulse in the sensed output at sensor 234 will occur, indicating that the syringe has reached home position. The home position, however selected, is such that, for example, the syringe may have been filled to an opereating level and may aspirate further to draw blood into the system through the valve. The amount of movement required to do this is carefully predetermined and the number of steps required of the stepping motor 240 driving nut to move the lag thread on the plunger will be repeated from one cycle to another. When valve position is changed, the plunger and syringe 50 may again be moved to discharge fluid through a different line to discharge the white blood cell sample into the container 28. Thereafter, the valve is repositioned so that further discharge of the diluent fluid from syringe 50 will clean either the aspirator tip or the vacutainer compartment as previously described. Finally, as the valve is repositioned to still another position, the syringe is moved back toward home so as to aspirate a predetermined amount of diluent into the system and be ready for another cycle.

The syringe 52 operates in exactly the same way, driven by stepping motor 244 through drive nut 242. "Home" is detected in this case using light source 235 and detector 236 through the plunger.

In connection with the rotary valve, the movable disc 164 moves to a different position in accordance with the program. Whether the blood is fed in through the aspirator tip or from a vacutainer, sensing means will detect the presence of a container and initiate a proper program of valve positions, including one for aspiration from that container. However, only one position, for example, the position in which the syringes are filled, may be selected as the home position. In this case, the disc 164 which may be provided by perforations through its outer, larger diameter edge, or by another system which employs a light source and a home detector sensor 184 to indicate when home position is reached. In that case, the alignment of the hole with the light on one side and the sensor on the other will indicate that the position has been reached. As a practical matter, refinements are provided whereby as the change takes place from non-illuminated to illuminated, home is recorded as being achieved. Home is always approached from the same direction so that a program may provide for by passing the hole so that it may be sensed on reversing the direction of movement from the proper side.

Once home has been recorded, then the motor 182 drives gear 178 to move gear 176 associated with the movable disc 164 to know predetermined positions by taking a predetermined number of steps in a predetermind direction for each move. The showing in this drawing is schematic and quite different from the showing in application Serial No. 675,378 which merely shows the scope of the concept. However, a program may be derived mathematically for moving the valve from one

operable position to another and when the number of steps and direction of each move is fixed, providing this information in memory enabling repeating the direction and steps required starting from home on each cycle in response to the proper sensed condition to proceed.

A typical stepping motor drive moves effectively in half steps, where a half step is equal to 0.1 degree of rotation. Thus, for 180 half steps or 90 full steps, 18 degrees of rotation will occur. The valve may be set, for example, to rotate 18 degrees, then 36 degrees, and movements are on this order of magnitude rather than a full rotation or even a half rotation.

Various test procedures may also be incorporated for periodic check of accuracy. For example, an algorithm may be provided to make sure that, after a predetermined number of steps, the home detector 184 senses no light. If it does, the drive has not worked and drive failure is reported at the output. However, assuming the drive works properly in the proper position, detector 185 should then sense light from source 187 through another hole in disc 164. If light is not sensed by either when the movable disc is in the position where detector 185 should sense light, then a problem exists, such as proper drive is not occurring. The program should then call for a reverse drive and repositioning at home. If a repeat of the test again shows improper positioning, the display should print out the nature of the misfunction. If the device

performs properly, it should proceed. Another test for proper operation is to cancel a sequence if the position sensor 185 provides no signal when the rotatable disc 164 is in an operating position. In that case, the valve should be returned to home and the sequence repeated with the same sample. Again, if the proper positioning is not obtained, the output display 18 should carry a message indicating the type of misfunction.

Backlash is always a concern as a source of error. Techniques to minimize backlash during automatic or manual processing are built into the programming for the instrument of the present invention. For example, in charging a syringe, the program may be designed to slightly overfill the syringe so that the fluid level goes back beyond standby. Then, in order to set the syringe at the standby position, in which the syringe is fully charged, the plunger must be moved in a direction to discharge part of the fluid back into the reservoir. The same kind of technique is provided with the rotary valve and in all of the systems the approach to home is always the same direction so that backlash does not cause an error.

Another technique that is followed in connection with the use of the intelligent controller in driving the stepping motors is to accelerate the motor slowly when starting and then decelerate the motor slowly as the end of the particular segment of movement is reached. The number of steps is preprogrammed so that

this is a very reliable technique to prevent fluid surges and overshooting by the driven component. As seen in Fig. 7, the pulses are initially spaced further apart and increased in frequency at such a rate as to permit linear increase of speed during acceleration, and the techniques reversed for deceleration. At maximum speed, the pulses are uniformly spaced. One reason for this precaution is to move the blood without breaking up the liquid to air interfaces. The profile seen in Fig. 7 can be applied to the stepper motor using the intelligent controller and thus efficiently and relatively rapidly accomplished the movement of the controlled element from one position to another without causing shock or damage to the blood cells, or otherwise disrupting the tests or overshooting positions.

The automatic programming through the microprocessor speeds routine cleaning functions. An automatic cleaning cycle is provided to clean the valve after each use and to clean the aspirator tip and the vacutainer input.

Calibration is perhaps the function most vital to the operation of the device. Calibration has to do with standardizing the instrument to known correct values. This is done by providing manipulation, changing results to provide a calibration factor or multiplier which corrects the respective counts. Common to the various calibration techniques described hereafter is the storage of calibration parameters in memory, although calibration can be taken away from the instrument computer, and done manually or by remote computer.

The instrument may be calibrated by using a

standard calibration sample and calibrating to the assayed values, or the calibration factors may be adjusted directly using the keyboard input.

One method of calibration is calibration with averages. The operator is able to use up to 100 tests, to calibrate the instrument. The microprocessor is programmed to automatically calculate the averages and the percentage coefficient of variation (CV%). The computer may compare automatically readings taken within a range of acceptable values. The computer can manipulate and edit data for quality assurance. Such automatic calculation reduces the errors caused by calibrating to a small data base and eliminates time consuming calculations.

The instrument may be programmed to recalibrate itself in accordance with averages taken from repeated tests. Alternatively, the operator can modify data according to his own version. It is also possible to literally manually change the calibration to any values. It is preferably required to input a security code at the keyboard 16 before the microprocessor will permit access enabling modification of the calibration. If desired, a security code may be required for access to other information, including test data, stored in memory, as well.

For any sensitive operations, the program may require that a security code may be entered so that access may be limited to cleared supervisory personnel. By controlling the number of people who can adjust the threshold or calibration values, chances are lessened that these values will be casually or inadvertently

adjusted or tampered with.

The security code may be a three digit code. Without use of the security code, the display will allow the count and the calibration factor to be viewed but not changed by an operator. Once that code is placed in the system at the properer time, access can be had to the calibration factor adjustment. Calibration may then be displayed in terms of the correction factor for each of the successive readings. A change may be made manually or automatically, for example, by using the results from other machines for a given sample or automatically by using averages of various samples. For example, a change can be cross-checked on different instruments to see whether results are consistent and adjustment made if results are not consistent. Checking on a single instrument using multiple samples and rejecting patterns deviating from a stated norm is another calibration technique which may prove satisfactory. For example, one way of handling calibration is to take the historical average of up to 100 recent tests which may be stored in memory. Either way, what is derived is a calibration factor, a multiplication factor by which the results of the instrument actual cell count are adjusted.

One method of calibration using patient data utilizes memory in an instrument provided with the capability of fully storing the results of the last hundred tests. Provision may be made for discarding those few tests that depart from a preestablished norm and then taking the average of the remaining tests for calibration.

Another method uses multiple run on the same sample. It is important not to have more than two to three percent coefficient of variation (CV%) error in reproducability on any given set of runs. The average and standard coefficient of variation capability of the instruction can be calculated before proceeding with calibration of the instrument.

To assure maximum statistical accuracy, in addition to calibration of the system, a given sample may be run multiple times: for example, run three times and then the output is taken as the average. Such a multiple run procedure may be part of the program provided the microprocessor in accordance with the present invention. What is developed by way of calibration is a factor by which results may be multiplied to give an actual or final read out.

The instrument also provides what may be termed floating average. It will store all data for up to the last 99 tests. Access to any of these tests may be accomplished using the ID number of a particular test. By using ID numbers for access, any of those tests identified at any time are subject to deletion. It is possible to make substitutions, interchanges, or any other type of computer manipulation among various tests, keeping data of each complete test together. The computer can determine what an average or mean value should be, for example, in accordance with an algorithm and can calculate and apply the standard deviation or coefficient of variation in any other accepted way in order to use the material for future

comparison purposes. The instrument also provides for recall of test by ID number, and ID number change. It permits the tests recalled to be modified in their normal sequence position or to be repositioned relative to one another and it permits interleaving of new tests relative to old ones. An ID number change can be made using the security code and, then using the recall, that ID throughout the system can be changed, if desired. The system is designed to recall, make a change and revert back. In accordance with its program, ID number may be accessed automatically through the use of bar codes or other types of automatic reader devices, as well as by key input.

An internal clock provides information on timing and can include the times when calibration occurs and when a test is run. Information on how much calibration was off can also be ascertained. It is even possible on the system to have a Bull algorithm included to aid in calibration.

As the diagram of Fig. 4 suggests, calibration may alternatively be accomplished from a remote processor terminal 262 through the modem 264. The remote processor is capable of remote control of calibration in any number of ways. It can use stored data from the apparatus being calibrated, it can require that apparatus to make specified runs and use that data alone, or in combination with other data, and it can provide the basis from other apparatuses it supervises including an average or use any other source available to the remote computer. The remote terminal also

permits remote change of the security number itself or any security controlled information in the apparatus computer by a security code which may be a three digit code. At the remote processor terminal, it is also possible to get data on individual tests by giving the security code and the code number for the individual patient. The data received back typically includes patient data such as average counts, number of samples and information relative to the time of each test and the time between calibrations. Information of the general nature on the microprocessor 250 as a data center, such as the daily value of the control, is also available at the remote terminal.

The instrument can automatically calibrate itself if the automatic-calibration option is selected. The unit will call the factory (via modem) with an internal preset phone number. It will then pass the parameters from the last test run or the averages, over the phone lines to the factory computer. The factory computer may ask for additional control material to be run. The calibration factors are then computed, within the factory computer, and sent back to the instrument. The operator will be informed when the calibration is complete.

Preferably a hard wired modem without accoutical material may be used, such as a Bell 103, or alternatively, a Bell 212. As an option, the modem may be a separate printed circuit card, or alternatively, hard wiring with standard chips to the interface.

Cell sizing is derived from the histograms,

providing a more sensitive means of deriving MCV and MPV. Platelet counts are monitored and automatically extended for counts below 40,000 to obtain enough statistical data to acquire the histogram. In rare instances, if macrocytic thrombocytes or microcytic erythrocytes are present, the instrument is capable of performing platelet counts on platelet-rich-plasma.

Fig. 8a shows a typical platelet size distribution curve. That is, the channels are indicative of platelet size, ranging from smaller to larger along the horizontal axis of the graph. The curve on a semi-log axis of platelet size distribution, as seen in Fig. 8b, is generally bell-shaped. For example, semi-long graph may be derived by taking the log of the input amplitude 312 as seen in Fig. 10. Distortions are encountered, however, because other particles of small size may occur in large numbers and overwhelm the sizing circuitry. Also, on the higher end, as seen in Fig. 8a, there can be confusion caused by overlap of larger particles in the blood, particularly red blood cells, which are not distinguishable from platelets in the count.

In accordance with the present invention, a cut off is made at selected ends of the normal curve for platelets within regions where other particles are not normally detected. Thus, a portion of the curve near the peak and down the slope on each side for a significant distance is taken as defining the shape of the curve. Then, based upon the typical shape of known platelet size distribution curves, the rest of the

shape is extrapolated. The number of platelets of each size can be determined by a taking a count from under the extrapolated curve, either total count, or channel by channel. In this way, interference from the small particles at one end and from the large red cells on the other can be ignored.

This can be done by plotting the logarithm of the counts in the various channels near the peak to derive a bell-shaped curve as seen in Fig. 8b, instead of the curve of Fig. 8a. The log v. Δ log curve should then provide an approximately straight line. Taking the straight portion of the curve from the peak region to extrapolate upwardly and downwardly by extending the straight line yields the straight line of Fig. 8c as a good approximation. This extrapolation can be done using the least squares fit formula, for example. Then, by reversing the process, the microprocessor can effectively reconstruct a proper curve to represent platelet distribution without noise and red blood cell interference.

It will be understood that in a normal situation the points obtained by taking the log of the counts in the various channels will not fall strictly along a straight line so that it is necessary to use the computer capabilities of the system to find a mean value straight line over a substantial distance and then extrapolate that line from where it begins to curve. Using this straight line technique there has to be some criterion about whether counts are taken or discarded. As a practical technique, the straight line

is generated from the peak out in each direction and since the peak has the most accurate information, that portion of the curve is given a weighted reliability. In determining the direction the straight line should take in deciding effectively which points to eliminate. Extreme points can be eliminated on a prearranged discard formula.

In the field, threshold values are subject to variation, like other parameters in blood testing. Changing the threshold values, however, requires access through the security code. These threshold values are particularly important because, in the event that a proper curve cannot be found, the threshold values will determine the platelet count. If the result of the process described is that predetermined criteria of a proper curve are not met, a "no fit" result is generated.

Every effort is made to generate the curve and this is done by using actual points determined by count measurement in the various channels, discarding points that are beyond a certain tolerance, then using the least square fit formula to select the straight line. If the solution simply cannot be found, a "no fit" result is generated and the default procedure takes over using the threshold values given for the platelet count. Some indication on the display or the print out will be given if this has occurred so that the user will be warned that a simulated threshold rather than actual data is used.

When the white blood count CBC is complete, a

differential count may be made which classifies each type of white cell. This is done with a microscope rather than with the instrument itself. However, the instrument is still of value in that the cell count can be input on the keyboard with the count being made in the conventional way by, for example, counting 100 cells and identifying each type. Effectively the instrument will count 20,000 to 30,000 cells to get a bigger statistical base with better accuracy and will sort and match the counts. Referring to Fig. 1, the differential values can be entered on the keys 17 of the hand held unit 15 designed to be plugged into the instrument and preferably on a sufficiently long connection cord for facilitating use at a remote position. Nevertheless, even with the larger cell count by instrument, the actual count is still made from the slide. The percentage is still the same but the absolute numbers for the volume is much improved. Also, seeing white cell ratios ahead alerts the operator to a possible problem.

Fig. 9 shows a preferred format for information that is printed out on a ticket showing blood test results. In addition to test information, the date and time are indicated by the internal clock. A print out of the distribution of platelets is shown.

Values out of the expected range are automatically flagged on the printout card. Each user may define his own expected values or use the default values.

Platelet (PLT) lower and upper valley alarms will indicate that the platelet histogram is out of normal

at one extreme or the other of the bell curve. This allows the operator to double check the validity of the results.

It should be noted that the printer can also be used to print out various other selected convenient formats of data. For example, a calibration format prints out adjusted calibration factors. Calibration can also be printed out with averages. Self test results can be printed out as well. Also, there can be a print out of critical volume percentages of each count. There are numerous other types of printouts relating to all aspects of testing and using the instrument.

Referring to Fig. 10, various circuits for making analog adjustments to counts are schematically illustrated in block diagram form. Parallel input circuits are provided for white blood count and red blood count beginning with a programmable current source 274a for the white blood count and 274b for the red blood count. These programmable current sources include a digital to analog converter (DAC) 276a for white and 276b for red blood cell circuits. The DACs regulate current sources 278a and 278b, respectively, to give a variable current output which may be manually or computer regulated. An actual white blood count and red blood count are input, respectively, to probes 280a and 280b. The counter pulse modulated signals are fed through preamplifiers 282a and 282b, respectively, and then through amplifiers 284a and 284b. White blood

cell count is here fed through an extra amplifier 284a' as well. The amount of amplification, of course, is a design consideration. The position of switch 286 determines whether the white or the red blood count signals will be fed to the base line restorer 288. The output of base line restorer 288 is divided and fed to input amplifier to the differential comparator 294. Comparator 294 is part of a programmable threshold 290. The control of the programmable threshold is digital to analog converter 292 which may be manually or computer controlled to respond to predetermined criteria to shift the count spectrum of the output to counter 296.

It will be appreciated by those skilled in the art that the circuit described thus far concerns counting of alternatively white blood cells and red blood cells. In the prior art, both the current source and the threshold for counting has been fixed. In accordance with the present invention with the circuit provided, the current source and the threshold for counting may each be adjusted under the control of the system computer. This adjustment permits the considered count spectrum to be shifted to whatever proves to be the optimum operating region. For example, if particles are small, the current may be increased and the threshold adjusted to compensate.

The mean corpuscular volume count (MCV) is obtained for red or white count, depending upon position of switch 286, by taking the output of the base line restorer (BLR) 288 as the input of an editor

amplifier 298. This, in turn, is processed through the linear gate 302 which feeds peak detector 304, a device which not only detects the peak or maximum but holds that amount until superceded by a greater level. The "mean" is derived by the system computer using an algorithm from the retained peak amounts which are successively output to analog to digital eight bit converter which feeds the computer.

Means is provided to assure that red and white cell counts are given adequate consideration. For example, switch 286 may be such a means which in practice may be an automatically operated device. The red cell sizes are supplied on a time available basis. Since there are many red cells present, only a sampling is necessary to determine the size distribution. The distribution is analyzed by the computer to find the mean corpuscular volume.

Output of the red blood cell amplifier 284b is fed into amplifier 308 of the platelet (PLT) count circuit which is fed through a further base line restorer 310 to a log amplifier 312. Log amplifier 312 provides more gain for the smaller particles to enable better detection. The output, in turn, is fed through a base line restorer (BLR) and filter (314), which may function to eliminate counts which are sufficiently off the curve to be disregarded. The output of the filter 314 is fed to a linear gate 316 then feeds it to a peak detector and hold device 318 which feeds an analog to digital eight bit analog to digital output 320 which

generates the points on the platelet (PLT) curve seen in Fig. 9.

Between the BLR 310 and the log amplifier 312, the count signal is taken off as an input to each of the operational amplifiers serving as upper limit detector (ULD) 324 and lower limit detector (LLD) 328. At the control terminal of the upper limit detector 324 a digital to analog converter (DAC) 322 sets the upper limit of the signal. The DAC 322 is controlled by the program of the computer and the DAC 322 output is fed to the upper limit detector amplifier 324 which also receives the incoming signal from BLR 310. If the threshold set by the digital to analog converter 322 is exceeded, an output is fed to the peak detector 318 to suppress pulses over the upper limit. Similarly, a lower limit detector (LLD) 328 is provided a computer controlled variable lower limit signal by digital to analog converter (DAC) 326, which is fed into the lower limit detector (LLD) 328 along the output signal from BLR 310. If the lower limit is exceeded, an output will occur and be fed to the peak detector 318 to suppress those pulses below the lower limit.

The log amplifier used in the PLT channel provides more gain for the smaller particles, such as platelets, and less gain for the larger ones, such as the red blood cells. This also yields a normal distribution for the platelets as opposed to a log normal distribution.

The platelets upper and lower limit discriminators 324 and 328 are under computer control so that they may

be adjusted through the DACs 322 and 326 by computer. Employing these discriminators eliminates from the output effectively useless information in such a way that the computer time is not needed for analyzing useless pulses.

Referring now to the HGB circuit for measuring hemoglobin, an input source digital to analog converter (DAC) 330 supplies a power amplifier 332 with a signal which regulates the intensity of lamp 230a. A sample is inserted between the lamp 230a and photodiode 230b so that different levels of signals for different samples may be compared with the signal level for a colorless fluid standard simialrly inserted. The photodiode output is put through an HGB amplifier 338, in parallel with resistor 340 and the amplifier output is supplied to the 12 bit analog to digital converter 342.

In the prior art use, lamp to photodiode systems have been used for measuring HGB. First, they measure the output of a blank then they measure the output of a sample and they take the difference. The present invention adds a computer in the loop to adjust the lamp output when the standard is present to bring the light output up to a predetermined standard intensity. By making the light output as high as possible, the signal to noise ratio the measurement is improved.

The nature of the computer control in accordance with the present invention has been briefly described. It will be understood that the computer is used in many conventional ways but also in many non-conventional ways in accordance with the present invention. The

microprocessor may be programmed to sequence the events, allowing for interruption or alternative actions in accordance with intermediate effects. The microprocessor may be programmed so that when there are problems at a particular juncture, some sort of alarm or warning is sounded or shown. If manual steps are required to implement the program, the required manual steps may be requested by a message on the screen provided for in the computer so that the operator will know what to do. Automatic steps may proceed without interference unless there is some problem as detected by various sensed abnormal conditions during tests, as well as by conditions which may be sensed at any time and displayed or which may be used to discontinue the tests and identify on the display the region of malfunction or reason for discontinuance if the problems created necessitate shut down. System alarms may be indicated by a message appearing on the display screen and/or may be indicated by some sort of an audible or visable alarm signal, such as a buzzer or a flashing light. The kind of situation in which a warning light or message should be provided, and interlocks provided to shut down the system, for example, is loss of vacuum in the internal waste tank, or exhaustion of the supply of diluent or the supply of lysing fluid or indication of inappropriate pressure, or some lack of function in response to program sequence such as blockage of an orifice.

The program may, for example, on the blockage of an orifice provide its own self-correction effort, such

as back flushing the orifice.

If the instrument determines that an aperture is clogged, an attempt will automatically be made to clear the clog and the test will be rerun. An automatic backflush at the jewel orifices of the cell counter at the end of each count is also provided to keep the aperatures free of protein buildup.

In the event that such technique does not work, however, a warning must be displayed and the system shut down.

Examples of a alarms and prompts provided for this instrument include the following:

1. Clog - no counts detected within count time
2. Overrange - if limits within units are exceeded
3. Underrange - if limits within units are not reached
4. Lyse Empty
5. Diluent Empty
6. Waste Full (only if container is used for waste)
7. Platelet lower Valley (excess of noise)
8. Platelet upper Valley (small red cells)
9. Main computer off line
10. Impedence
11. No Fit
12. Time

Some of the many diagnostic tests that can be manually run by the operator are as follows:

a.) Date and time change

b.) Security code change

c.) Electronic background test (injecting known signal)

d.) Repeat counts of the same dilution

e.) Leak test

f.) Expected values

g.) Sequential number

h.) Display check

i.) Keyboard check

j.) Printer check

These tests enable either diagnostic information from the computer to be printed out or result in one of the foregoing alarms and prompts to occur.

Various types of applications of the computer to the present invention have been discussed. It will be understood by those skilled in the art that the techniques described are representative and that many variations are possible as well as other uses of the computer. It is anticipated that other applications for the same computer will be found by those skilled in the art. The claims are intended to include the many variations within the scope and spirit of the present invention.

CLAIMS

What is claimed is:

1. In a blood cell counting apparatus a fluid system comprising:

separate intake means in cooperation with separate fluid supplies enabling drawing fluids into the system from a plurality of supplies;

outlet means permitting discharge of fluids from the system;

syringe means having a movable plunger for alternately drawing fluids into the system and expelling them through the outlet means;

valve means alternately connecting the syringe means to the respective intake means and to the outlet means; and

tubing connecting the system together;

a drive means coupled to the plunger of the syringe to move it either direction along movable operating path;

means for putting the plunger in a preselected home position; and

drive means in a predetermined direction and stop the drive means at a predetermined position so that the plunger assumes a predetermined position relative to home position.

2. The apparatus of claim 1 in which the drive means is a stepping motor, the power source is a pulse source and the means that assures that the drive means stops in predetermined position is a power source to drive the drive means including means taht assures that

the drive means stops in precise predetermined position.

3. The blood cell counting apparatus of claim 1 in which sensing means is provided to sense when the plunger is in home position.

4. The blood cell counting apparatus of claim 1 in which the program means effectuates various successive movements of the plunger to accomplish all the steps necssary to complete a selected blood test.

5. A method of metering a precise amount of fluid aspirated or dispensed by a syringe comprising;

positioning the syringe plunger in a known position,

driving the plunger away from that position in a preselected direction using a stepping motor,

counting pulses driving the stepping motor, and

stopping the motor and the plunger at a program selected position after counting a predetermined number of pulses.

6. The method of claim 5 in which after stopping the plunger at the program selected position, the direction of the stepping motor is reversed and pulses driving the stepping motor in the opposite direction are counted and the motor and the plunger are stopped at another program selected position after counting another predetermined number of pulses, whereby, in one direction of plunger movement, the syringe aspirates and, in the other, it dispenses.

7. In a blood cell counting apparatus employing a multi-position movable valve having a movable member positionable in a plurality of functional positions;

a detector to sense when the movable member is in home position,

a stepping motor drive means coupled to and driving the movable member,

a pulse source to drive the stepping motor,

counter means to count the pulses fed to the stepping motor,

program means to actuate the stepping motor in a predetermined direction and stop the stepping motor in predetermined functional valve position after a predetermined number of pulses.

8. The apparatus of claim 7 in which the drive means is a stepping motor, the power source is a pulse source and the means that assures that the drive means stops in predetermined position is a power source to drive the drive means including means that assures that the drive means stops in precision predetermined position.

9. The blood cell counting apparatus of claim 6 in which the program means is made responsive to completion of the procedures at each successive position of the movable valve to initiate each new move of the movable valve by actuation of the stepping motor in a predetermined direction and stopping the stepping motor after a predetermined number of steps.

10. A method of positioning a valve having multiple operating positions of a movable valve member

driven by a stepping motor comprising;

sensing when the movable valve member is in a known position,

driving the movable member in a program selected direction toward a predetermined position,

counting pulses driving the stepping motor, and

stopping the motor and movable member at the program selected position after counting a predetermined number of pulses.

11. The method of claim 10 in which the movable valve member starts from a home position and moves to a program selected position, the motor is stopped after a predetermined number of steps from home, a home sensor is checked and, if there is no home signal indicating that the movable member has departed from home position, the motor is reactivated and the program proceeds, but, if the check reveals that the movable member has not moved from home, an alarm is generated.

12. The method of claim 10 in which a program is provided for successive repositioning of the movable valve member from one operating position to the next, wherein the program determines the direction and the number of steps taken by the stepping motor.

13. The method of claim 12 in which a program is provided which is responsive to completion of a function at a particular valve position to automatically initiate the move to the next valve position.

14. The method of claim 12 in which the program

also repositions the valve at home at the end of a programmed series of movements.

15. The method of claim 12 in which, at each programmed stop position, sensor means is used to detect indicia to determine that the valve is actually in an operating position, and, if it is not at an operating position, a misfunction is indicated.

16. The method of claim 15 in which, if such non-operating position of the valve is sensed, the stepping motor is actuated to cause the valve to return to home and repeat the test including the stepwise movements of the movable member of the valve.

17. The method of claim 12 in which a variety of programs providing for a variety of movable valve member repositionings are provided, the program being selected to suit the particular kind of test being performed.

18. The method of claim 17 in which the appropriate program is selected automatically by means sensing the parts of the instrument being employed by the user.

19. In a blood cell counting apparatus having a fluid system comprising;

separate intake means in cooperation with separate fluid supplies enabling drawing fluids into the system from a plurality of alternate supplies, including diluent supply,

outlet means permitting discharge of fluids from

the system,

syringe means having a movable plunger for alternately drawing fluids into the system and expelling them through the outlet means,

valve means alternately connecting the syringe means at least to diluent supply or to the blood sample or to the outlet means, and

tubing connecting the system together,

drive means for controlling at least the directions of movement and stop positions of the syringe means and the valve means,

computer means for controlling the sequence and operation of the system and having at least input means providing program sequence and operation instructions to the computer to position the syringe means and the valve means in sequential positions determined by a program requiring performance of a sequence of steps necessary to the specific blood test requested by the input means; and

display means displaying output and intermediate instructional information.

20. The blood cell counting apparatus of claim 19 in which signals from position sensing means are fed back to the computer means to sense whether the valve means has stopped at predetermined positions.

21. The blood cell counting apparatus of claim 20 in which stepping motors are employed to drive plungers of the syringe means and the valve means, a pulse source is provided for generating pulses to drive the stepping motors, counter means is provided to count the pulses to the respective stepping motors, and means to

provide to stop pulses to the stepping motors in accordance with the program requirements for positioning the valve and the syringes.

22. The blood cell counting device of claim 19 in which a program is provided in which pulses gradually increase in frequency so as to bring the speed up to maximum, maintain it at the desired maximum, and then gradually decrease frequency so as to gradually slow the motor before the last pulse following which the motor stops.

23. The method of determining curve shape in a blood particle log normal size distribution curve comprising;

taking the logarithm of the blood cell input amplitudes enabling plotting of a curve of generally symmetrical bell shape,

generating a straight line from a plot of change of logarithm (Δ log) of counts against the logarithm of blood cell input amplitudes, giving more weight to those points near the peak of the second curve in determining line slope, and

reversing the process using the straight line to regenerate ultimately a curve showing a distribution of number of particles against particle size.

24. The method of claim 23 in which an average is derived by mathematical manipulation of the derived curve.

25. The method of claim 23 in which the effect of the method steps is to eliminate interference between

red blood cells, platelets and noise.

26. The method of claim 23 applied to platelet count.

27. The method of claim 23 applied to mean platelet volume (MPV) including the additional step of finding from the ultimately regenerated curve the mean platelet volume which is mathematically the average platelet volume.

28. The method of determining curve shape for mean cell volume (MCV) in a blood particle normal size distribution curve comprising;

generating a straight line from a plot of change of logarithm (Δ log) of counts against the normal, giving more weight to those points near the peak of the curve in determining line slope, and

reversing the process using the straight line to regenerate ultimately a curve showing a distribution of number of particles against particle size.

29. The method of determining curve shape for red blood count (RBC) in a blood particle normal size distribution curve comprising;

generating a straight line from a plot of change of logarithm (Δ log) of counts against the normal, giving more weight to those points near the peak of the curve in determining line slope, and

reversing the process using the straight line to regenerate ultimately a curve showing a distribution of number of particles against particle size.

30. The method of claim 28 in which a red blood cell count is completed by integrating or summing up all counts under the ultimate regenerated curve.

31. The method of claim 28 in which a mean corpuscular volume count is computer by taking the average of all counts under the ultimate regenerated curve.

32. The method of approximating curve shape in a blood particle log normal size distribution curve comprising;

taking the logarithm of the blood cell input amplitudes enabling plotting a count distribution curve of generally symmetrical bell shape,

using the least squares fit formula to generate a straight line, the straightness of which permits examining the log curve for its uniformity, and

if the curve does not measure up to predetermined minimum requirements using raw data to generate the count between two predetermined threshold limits.

33. The method of claim 32 done by computer, wherein counts are first subjected to a logarithm translation by a log amplifier and standards are stored for comparison together with predetermined tolerances for acceptance and rejection.

34. A method of using an instrument for making specified blood cell counts using a computer comprising:

establishing a minimum count limit within the computer for minimum acceptable counts for various

kinds of blood counts,

making a count of a particular kind, and

rejecting the count if the threshold is not exceeded for that particular kind of count.

35. The method of claim 34 for making a plurality of blood counts using a computer in which the minimum count limit may be changed for any count by use of an access code input.

36. The method of claim 35 in which, during a test cycle, background noise is observed and thresholds are adjusted to compensate for the background noise.

37. In a blood cell counting instrument for making various blood counts having apparatus for receiving blood samples, diluting the samples, and making counts, and including counter means for recording counts as they occur, computer means to at least store such counts, and display means, the improvement comprising a differential input keyboard connected with the system and capable of enabling manual input of counts of various types of white blood cells as they are observed by the keyboard operator.

38. In a blood test apparatus having blood count apparatus, a calibration system for blood count data and a computer to calculate various counts including memory for storing calibration parameters, the improvement of providing security code access to that memory and means to modify the calibration parameters upon achieving access.

39. In a blood test apparatus employing computer means, a calibration system comprising:

means for providing an independent count result from a specified blood sample not from the apparatus,

means for recording at least one count result from the apparatus under calibration, and

computer means for determining a multiplication factor from the ratio of the two count results by which further count results from apparatus under calibration may be multiplied to calibrate the apparatus.

40. The apparatus of claim 39 in which the independent count result is compared with the average of at least three runs from the same sample.

41. The apparatus of claim 39 in which the independent count result is compared with an average of stored test results from the apparatus for multiple samples.

42. The apparatus of claim 39 in which the independent count result is derived from measurements of another calibrated instrument.

43. The apparatus of claim 39 in which the independent result is generated from use of a standardized control material.

44. The apparatus of claim 39 in which the independent result is generated from known results on a large population of patients.

45. The apparatus of claim 42 in which the

independent count result is derived from the average of multiple tests on other instruments.

46. A method of calibrating blood count apparatus having calibration factors stored in a computer memory comprising

providing an access code to the computer permitting access to the calibration factors in memory, and

modifying the calibration factors manually through an input keyboard.

47. The method of calibrating blood count apparatus capable of storing successive blood counts in a computer memory of a blood test instrument comprising;

storing successive blood count results in memory,

applying an algorithm in the computer to averaging a predetermined number of counts,

comparing the average with a known accurate result to derive a new calibration factor; and

replacing stored calibration factor with said new factor.

48. The method of calibrating blood count apparatus having calibration factors stored in a computer memory of a blood test instrument comprising applying an algorithm to the results of the last test run in memory run to derive new calibration factors, and applying those calibration factors to the next test.

49. The method of remotely calibrating blood test

apparatus having calibration factors stored in an apparatus memory, comprising;

providing a link between the apparatus and a remote computer,

passing test results from the apparatus to the computer,

applying a calibration algorithm in the computer to the test results received from the apparatus to derive new calibration factors, and

sending back to the apparatus memory the recalibrated calibration factors for use in the apparatus.

50. The method of claim 49 in which the test results supplied are test results run at the request of the remote computer.

51. The method of claim 49 in which the test results supplied are those of a predetermined number of prior tests stored in the apparatus memory.

52. The method of claim 49 in which the link provided includes telephone lines and the blood test apparatus has means capable of telephone dialing to access the computer over telephone lines and means to interrupt the telephone line connection following recalibration.

53. A blood test apparatus, comprising;

means to perform various blood counts,

means to input an identification number for each blood test,

means for calculating various blood test results,

means for storing a predetermined number of tests in memory with identification numbers,

means to access and display previous tests, and

means for selectively making changes to the record in memory.

54. The apparatus of claim 53 in which changes can be made only after a code is input to allow the means for selectively making changes to function.

55. The apparatus of claim 54 in which sequence of tests may be changed.

56. The apparatus of claim 54 in which identification members may be changed.

57. The apparatus of claim 54 in which specific test results may be changed.

58. The apparatus of claim 54 in which specific test results may be deleted from memory, new tests may be inserted or substituted.

59. Analog circuit control means for a blood cell counter comprising;

a programmable current source input including an adjustable digital to analog converter controlled by the computer,

a cell count signal input providing impulses representative of cell count for modulating the current source, and

counter means for counting the pulses.

60. The analog control circuit means of claim 59 in which the programmable current source is adjustable by a computer.

61. The analog control circuit means of claim 59 in which a programmable threshold means is provided prior to the counter comprising digital to analog converter means providing a control input to a comparator so that counter pulses exceeding the threshold at the comparator may be selectively eliminated by the comparator, said digital to analog converter being adjustable by the computer to adjust the threshold of the comparator.

62. The analog control circuit means of claim 61 in which the threshold established by the digital to analog converter is adjustable by a computer.

63. The counter control of claim 62 in which parallel programmable current sources are provided for the white blood counts and red blood counts, with cell count signal inputs and separate amplifier means, and a switch alternatively selecting white blood or red blood count input to the comparator and the counter.

64. A count circuit device for use with a cell counting circuit device employing a computer comprising:

a programmable current source input including a digital to analog converter controlled by the computer and a current source regulated by the digital to analog converter, responsive to means sensing pulses representative of cell counts, modulating the regulated

current, amplifier means to bring the signal to a usable level, a peak detector and hold device for determining the values along the curve from which mean values can be calculated, and an analog to digital read out device.

65. The device of claim 64 in which inputs are provided for both white and red blood counts through separate programmable current sources and separate probes, switch means selecting one of said devices or the other to be fed to the peak detector and hold device.

66. A platelet counter circuit comprising;

a programmable current source including a digital to analog converter controlled by a program supplying a current source regulated by the digital to analog converter,

a probe sensing pulses representative of red blood count for modulating the output of the current source,

suitable amplifier means receiving the modulated signal and amplifying it, and

a log amplifier converting the signal to a log scale along the axis representing size of particles,

a peak detector and hold device to determine the peaks of various size particle count,

a pair of threshold setting devices for setting the upper limit and the lower limit of the counts, each of said detectors being fed by the same pulse signal fed to the peak detector and hold device, the circuit to the respective upper and lower limit detectors being divided to feed an upper limit detector and a lower limit detector each of which is an operational

amplifier adjusted by a digital to analog converter to set a threshold for an upper or lower limit of particle size range respectively, said digital to analog converter receiving a digital to analog signal setting variable upper and lower limits, and

feedback connections to the peak detectors, respectively, from the upper and lower limit detectors determining the upper and lower limits of signals which are passed through the peak detector and appear at the analog to digital output for platelet count.

67. The platelet counter circuit of claim 66 in which the threshold selection is made in such a manner as to conserve computer time and capacity.

68. A hemoglobin detector comprising an analog to digital converter feeding a power amplifier with a signal, a light source which is connected to the power amplifier for regulating the intensity of the light source, a photo sensor optically coupled to the light source across a gap to allow passage of light through a sample or alternatively through a standard placed in the gap, an amplifier and analog to digital converter means to convert the output of the photosensor into digital form facilitating keeping the various comparative readings and calculating hemoglobin.

69. The system of claim 68 in which a feedback signal to the digital to analog converter through the computer keeps the output signal when the standard is interposed at a constant level and retains that same level of brightness through the inner position of the sample.

70. In a blood cell counting apparatus employing a computer, the method of assuring more accurate results comprising;

comparing final and intermediate results with predetermined normal ranges for each particular result and if any of the result deviates from the normal ranges, then rerunning the test.

71. In the method of claim 70, determining possible cause of the deviation, and taking corrective action before rerunning the test.

72. The method of claim 70 in which before rerunning the test, the computer makes certain tests of the computer and various instrument locations using built in test capabilities and, if the tests indicate correctable problems, correction those problems, but if the tests indicate uncorrectable problems, indicating an error signal.

73. The method of claim 72 in which the error signal identifies the source of the error.

AMENDED CLAIMS

[received by the International Bureau on 10 November 1986 (10.11.86) original claims 1,2,19,20 and 22 cancelled; claims 3,4 and 21 amended; other claims unchanged (5 pages)]

What is claimed is:

1. Cancelled.

2. Cancelled.

3. (amended) In a blood cell counting apparatus having a fluid system comprising;

separate intake means in cooperation with separate fluid supplies enabling drawing fluids into the system from a plurality of alternate supplies, including diluent supply,

outlet means permitting discharge of fluids from the system,

syringe means having a movable plunger for alternately drawing fluids into the system and expelling them through the outlet means,

valve means alternately connecting the syringe means at least to diluent supply or to the blood sample or to the outlet means,

sensing means to sense the plunger positions in the syringe including a home position;

tubing connecting the system together,

drive means for controlling at least the directions of movement and stop positions of the syringe means and the valve means,

computer means for controlling the sequence and operation of the system and having at least input means providing program sequence and operation instructions to the computer to position the syringe means and the valve means in sequential positions determined by a program requiring performance of a sequence of steps necessary to the specific blood test requested by the input means and receiving signals from the syringe piston sensing means to calculate when the plunger is stopped at home position; and

display means displaying output and intermediate instructional information.

4. (substitute) The blood cell counting apparatus of claim 3 in which a stepping motor is employed to drive the syringe plunger, a pulse source is provided for generating pulses to drive the stepping motor, counter means is provided to count the pulses to the stepping motor, and a program is provided in which when home is sensed additional pulses will be provided to drive the motor beyond home such that the syringe will be slightly overfilled and pulses will be provided to drive the motor in the reverse direction back to home discharging part of the fluid back into the reservoir in order to eliminate backlash and to provide proper filling at home position.

5. A method of metering a precise amount of fluid aspirated or dispensed by a syringe comprising;

positioning the syringe plunger in a known position,

driving the plunger away from that position in a preselected direction using a stepping motor,

counting pulses driving the stepping motor, and

stopping the motor and the plunger at a program selected position after counting a predetermined number of pulses.

6. The method of claim 5 in which after stopping the plunger at the program selected position, the direction of the stepping motor is reversed and pulses driving the stepping motor in the opposite direction are counted and the motor and the plunger are stopped at another program selected position after counting another predetermined number of pulses, whereby, in one direction of plunger movement, the syringe aspirates and, in the other, it dispenses.

also repositions the valve at home at the end of a programmed series of movements.

15. The method of claim 12 in which, at each programmed stop position, sensor means is used to detect indicia to determine that the valve is actually in an operating position, and, if it is not at an operating position, a misfunction is indicated.

16. The method of claim 15 in which, if such non-operating position of the valve is sensed, the stepping motor is actuated to cause the valve to return to home and repeat the test including the stepwise movements of the movable member of the valve.

17. The method of claim 12 in which a variety of programs providing for a variety of movable valve member repositionings are provided, the program being selected to suit the particular kind of test being performed.

18. The method of claim 17 in which the appropriate program is selected automatically by means sensing the parts of the instrument being employed by the user.

19. Cancelled.

20. Cancelled.

21. (amended) In a blood cell counting apparatus having a fluid system comprising;

separate intake means in cooperation with separate fluid supplies enabling drawing fluids into the system from a plurality of alternate supplies, including diluent supply,

outlet means permitting discharge of fluids from the system,

syringe means having a movable plunger for alternately drawing fluids into the system and expelling them through the outlet means,

valve means alternately connecting the syringe means at least to diluent supply or to the blood sample or to the outlet means,

tubing connecting the system together,

stepping motor drive means for controlling at least the directions of movement and stop positions of plungers of the syringe means and the valve means,

a pulse source for generating pulses to drive the stepping motors,

counter means to count the pulses to the respective stepping motors,

computer means for controlling the sequence and operation of the system and having at least input means providing program sequence and operation instructions to the computer to position the syringe means and the valve means in sequential positions determined by a program requiring performance of a sequence of steps necessary to the specific blood test requested by the input means and to stop pulses to the stepping motors in accordance with the program requirements for positioning the valve and the syringes of the program

driving at least one of the stepping motors providing pulses which gradually increase in frequency so as to bring the speed up to maximum, then continue at maximum rate to maintain speed at the desired maximum, and then gradually decrease frequency so as to gradually slow the motor before the last pulse following which the motor stops; and

display means displaying output and intermediate instructional information.

22. Cancelled.

23. The method of determining curve shape in a blood particle log normal size distribution curve comprising;

taking the logarithm of the blood cell input amplitudes enabling plotting of a curve of generally symmetrical bell shape,

generating a straight line from a plot of change of logarithm (Δlog) of counts against the logarithm of blood cell input amplitudes, giving more weight to those points near the peak of the second curve in determining line slope, and

reversing the process using the straight line to regenerate ultimately a curve showing a distribution of number of particles against particle size.

24. The method of claim 23 in which an average is derived by mathematical manipulation of the derived curve.

25. The method of claim 23 in which the effect of the method steps is to eliminate interference between

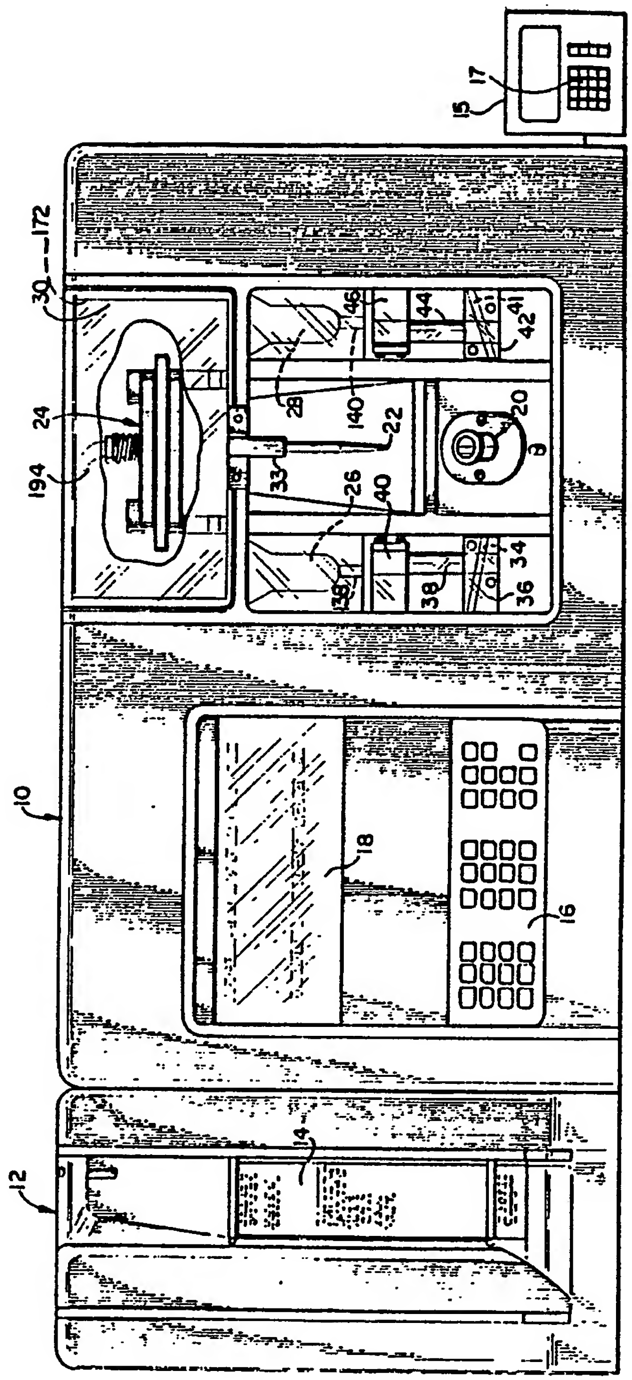

15
17
172
30
194
24
46
44
41
42
28
140
22
20
33
26
40
34
138
38
36
10
18
16
12
14

FIG. 1

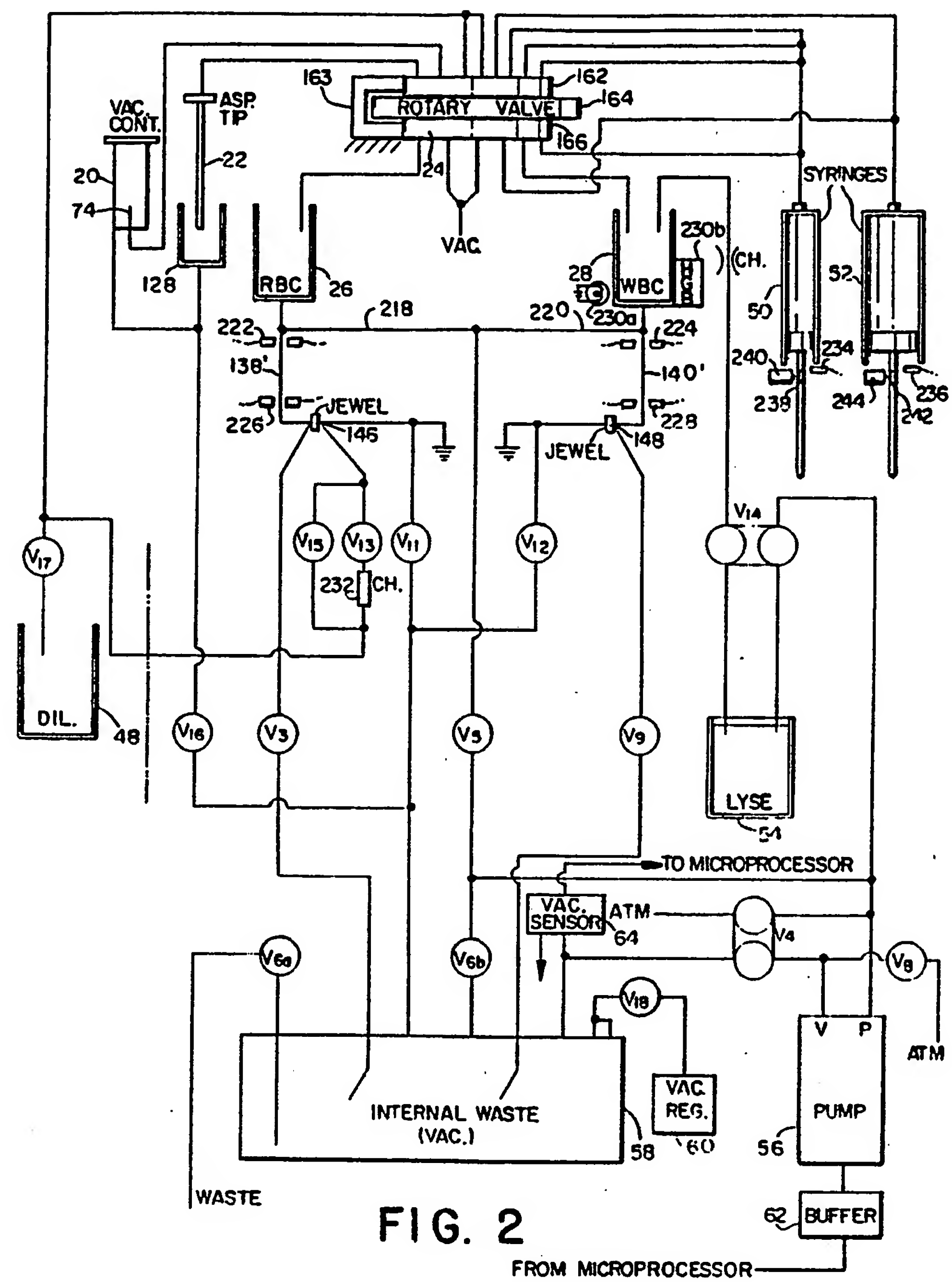

ROTARY VALVE
163
162
164
166
24
VAC.
VAC. CONT.
ASP. TIP
22
20
74
128
RBC
26
218
WBC
28
230b
230a
HGB
CH.
220
222
224
138'
140'
226
228
JEWEL
146
148
SYRINGES
50
52
240
234
238
244
236
242
V14
V15
V13
V11
V12
V17
232
CH.
DIL.
48
V16
V3
V5
V9
LYSE
54
TO MICROPROCESSOR
VAC. SENSOR
64
ATM
V4
V6a
V6b
V18
V8
V
P
ATM
INTERNAL WASTE (VAC.)
58
VAC. REG.
60
PUMP
56
WASTE
62
BUFFER
FROM MICROPROCESSOR

FIG. 2

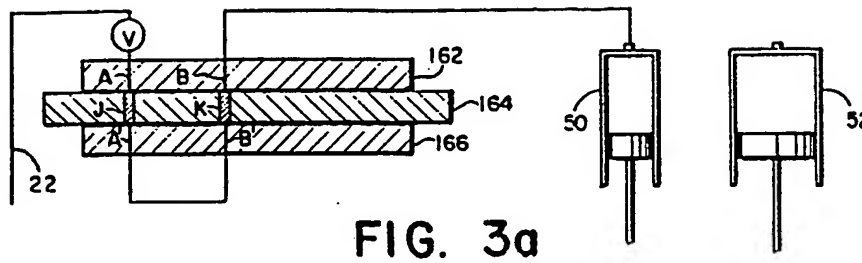


FIG. 3a

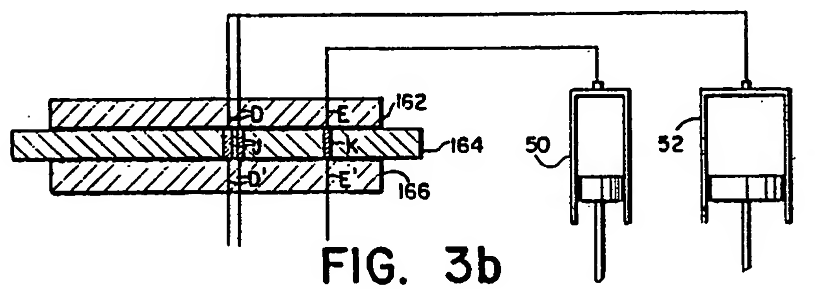


FIG. 3b

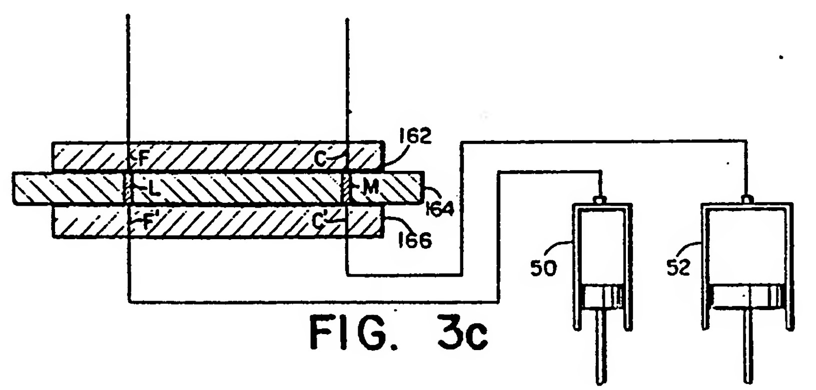


FIG. 3c

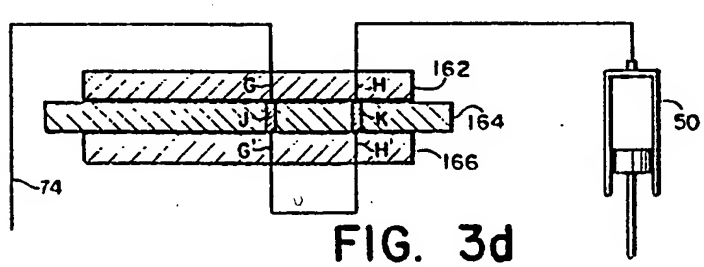


FIG. 3d

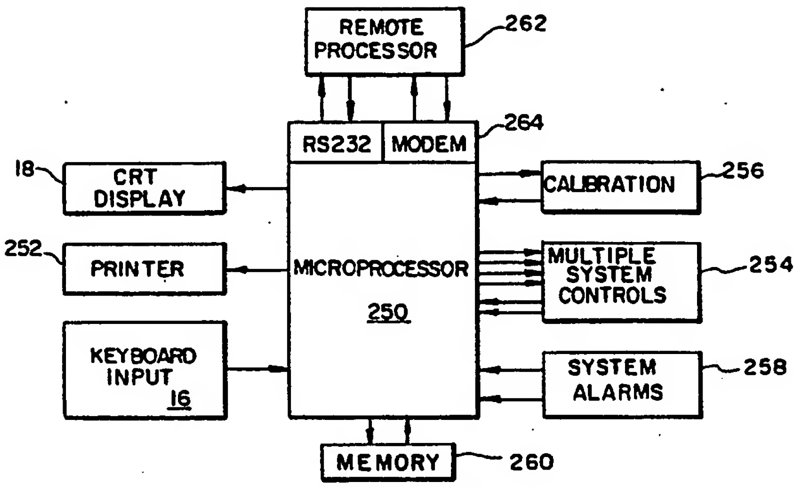


FIG. 4

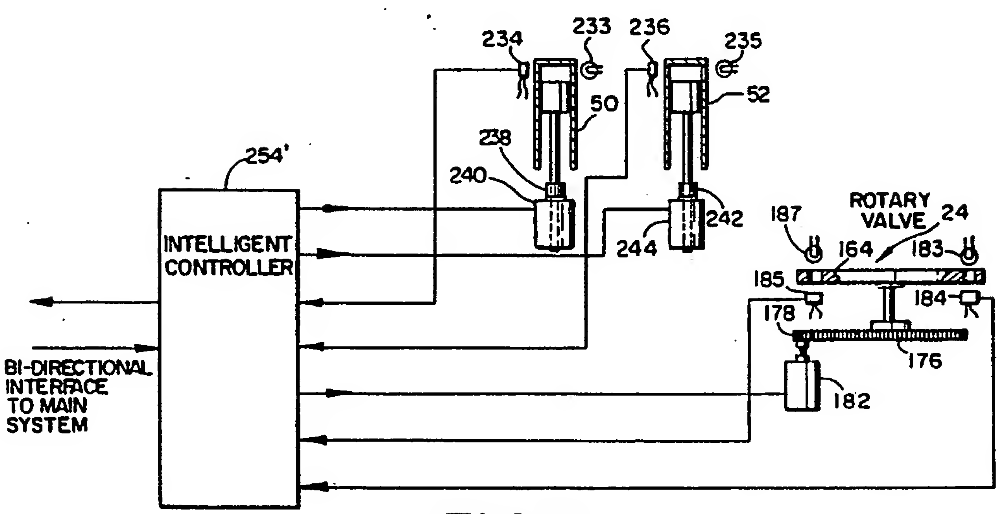


FIG. 6

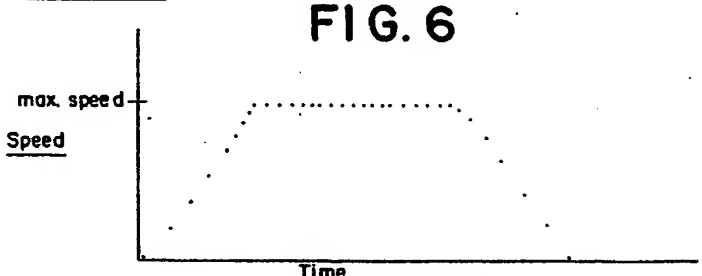


FIG. 7

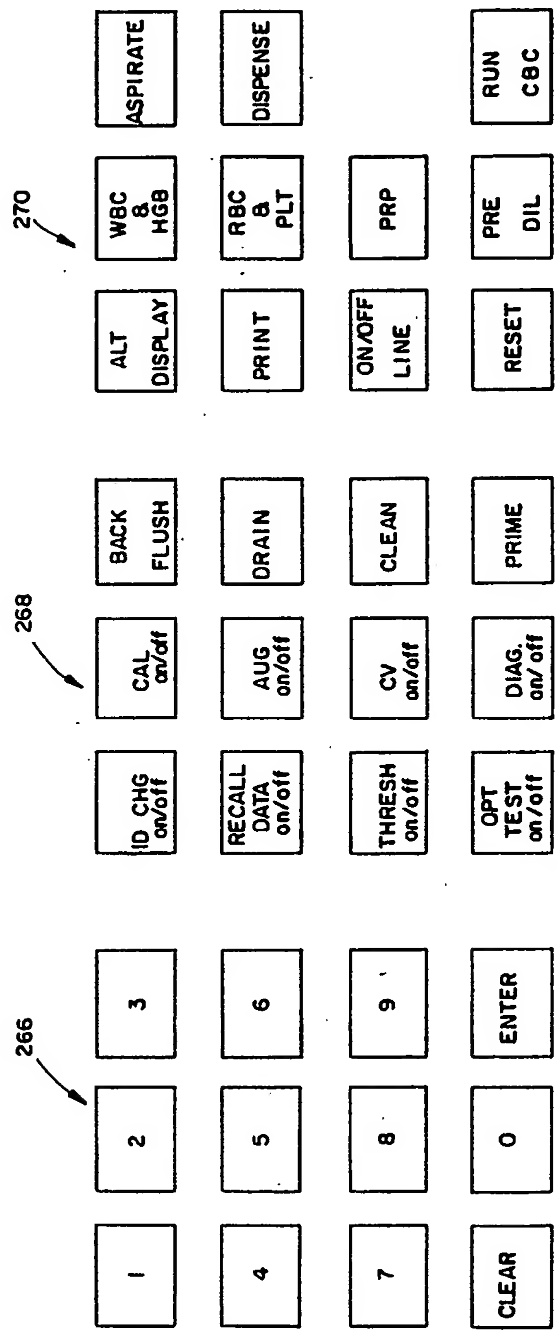

270
ASPIRATE
DISPENSE
RUN CBC
WBC & HGB
RBC & PLT
PRP
PRE DIL
ALT DISPLAY
PRINT
ON/OFF LINE
RESET
268
BACK FLUSH
DRAIN
CLEAN
PRIME
CAL on/off
AUG on/off
CV on/off
DIAG. on/off
ID CHG on/off
RECALL DATA on/off
THRESH on/off
OPT TEST on/off
266
3
6
9
ENTER
2
5
8
0
1
4
7
CLEAR

FIG. 5

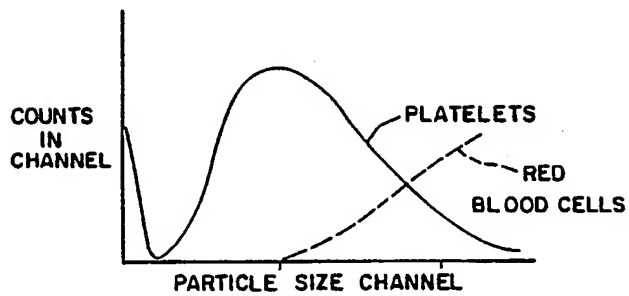


FIG. 8a

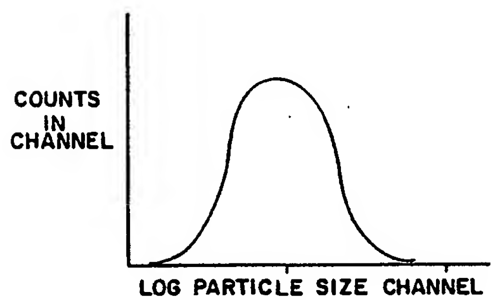


FIG. 8b

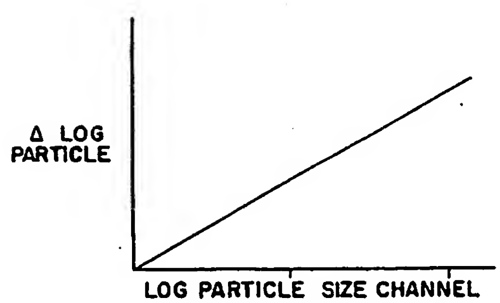
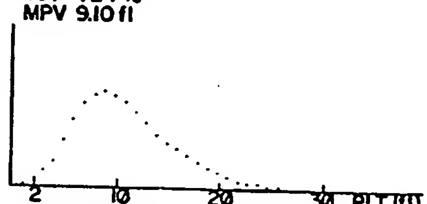


FIG. 8c

CELLTRAK-2200

---CBC RBC/PLT----- WBC/HGB---PRP---DIFF
REQ'D BY-------------- DATE--------
DATE 11/08/84 TIME: 07:55
ID #000001
WBC 6.3THOU
RBC 4.30 MIL
HGB 13.0 g/dl
HCT 39.0 %
MCV 90.0 %
MCH 30.2%
MCHC 33.3%
PLT 260. THOU
TCT .24%
MPV 9.10 fl



DIFFERENTIAL			MORPHOLOGY	
Seg	---%	----Thou	Polychrom	---
Band	---%	----Thou	Hypochrom	---
Lymph	---%	----Thou	Poik	---
Mono	---%	----Thou	Target	---
Eosin	---%	----Thou	Sphero	---
Baso	---%	----Thou	Aniso	---
Atyp			Micro	---
Lymph	---%	----Thou	Macro	---
-----	---%	----Thou	Basco Stip	---
-----	---%	----Thou	Vacuoles	---
-----	---%	----Thou	Toxic Gran	---
nRBC	---%		PLT	---

FIG. 9

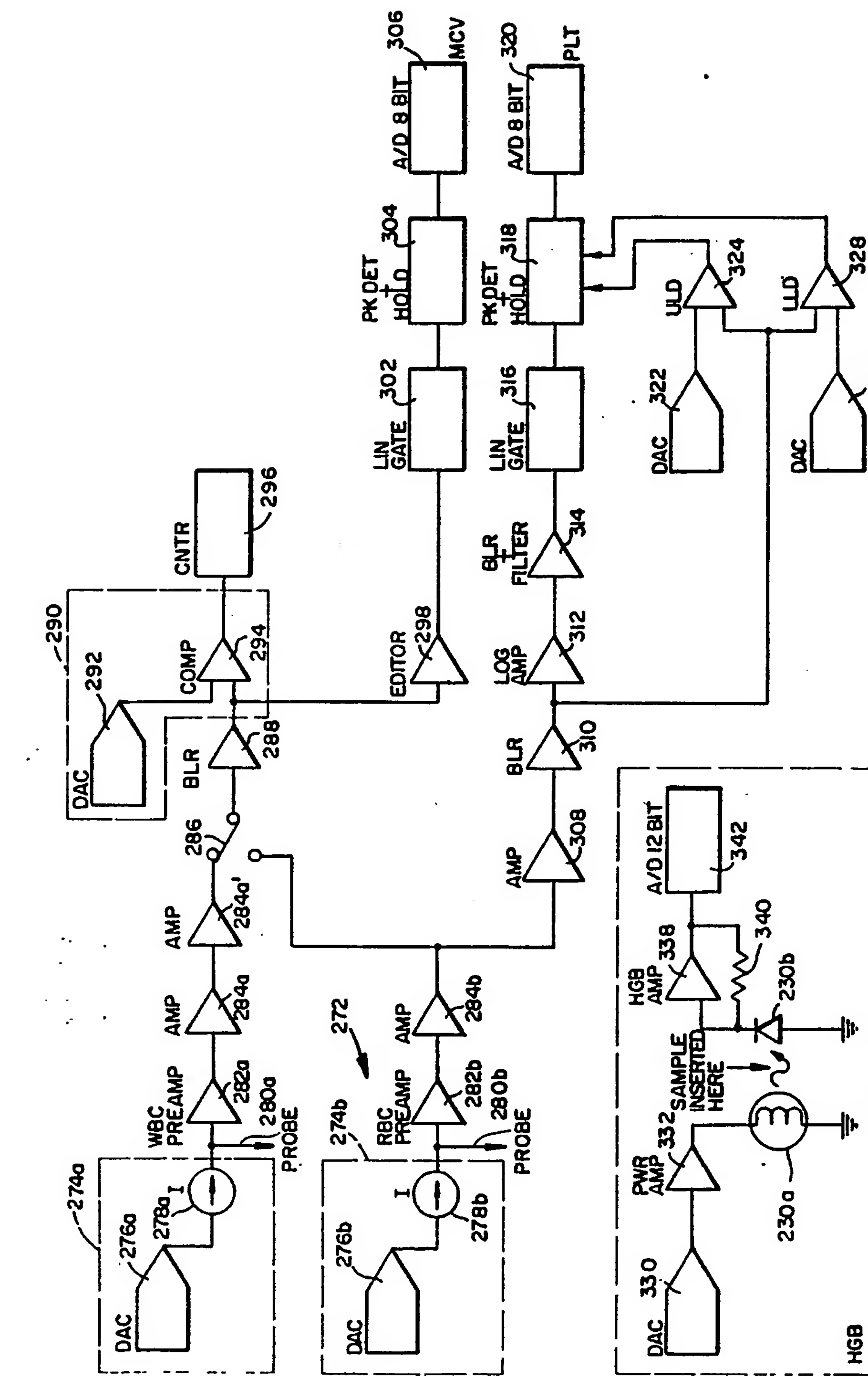

DAC
276a
278a
I
274a
WBC PREAMP
282a
280a
PROBE
AMP
284a
284a'
286
BLR
288
290
DAC
292
COMP
294
CNTR
296
EDITOR
298
LIN GATE
302
PK DET + HOLD
304
A/D 8 BIT
306
MCV
272
DAC
276b
278b
274b
RBC PREAMP
282b
280b
284b
308
310
LOG AMP
312
BLR + FILTER
314
316
318
A/D 8 BIT
320
PLT
DAC
322
ULD
324
326
328
HGB
DAC
330
PWR AMP
332
SAMPLE INSERTED HERE
230a
230b
HGB AMP
338
340
A/D 12 BIT
342

FIG. 10

INTERNATIONAL SEARCH REPORT

International Application No PCT/US86/01350

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(4) GOIN 15/12, GOIN 35/00
US 422/67, 422/100, 364/555, 364/573

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	73/864.12, 864.14 324/71.4 221/113, 119, 222/135, 144.5 377/2, 11, 21 364/554, 555,573 422/63-67, 73, 100, 103 436/63

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [6]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
X Y	US, A, 4,333,356 (BARTELS) 08 June 1982, see entire document	1,2,4,19,22 3,20,21
Y	JP, A, 58-87462(A) (ABE) 25 May 1983, see figures 1-3	1-4,19-22
Y	US, A, 4,448,752 (BANNO) 15 May 1984, see column 2	1-4,19-22
X Y	US, A, 4,058,367 (Gilford) 15 November 1977, see column 1 lines 21 to 68, column 2 lines 1-4, figure 1.	37,53-58 37,53-58, 70-73
Y	US, A, 4,030,888 (YAMAMOTO) 21 June 1977, see entire document	37,53-58
Y	US, A, 4,043,756 (SOMMERVOLD) 23 August 1977, see entire document	37,53-58
Y	US, A, 4,412,175 (MAYNAREZ) 25 October 1983, see column 4 lines 11-25.	34-36
Y	US, A, 4,447,883 (FARRELL) 08 May 1984, see entire document	34-36
Y	US, A, 3,133,445 (RICHARD) 19 May 1964, see entire document	23-33
Y	US, A, 3,939,459 (HOOPES) 17 February 1976, see entire document	23-33
Y	US, A, 4,063,309 (HENNESSY) 13 December 1977, see entire document	27-28,31

* Special categories of cited documents: [15]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
28 August 1986	10 SEP 1986
International Searching Authority [1]	**Signature of Authorized Officer [20]**
ISA/US	Michael S. Marcus Michael S. Marcus

Form PCT/ISA/210 (second sheet) (May 1986)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

A	US, A, 3,557,352 (HOGG) 19 January 1971, see entire document	23-37,70-73
A	US, A, 3,473,010 (BLOOMFIELD) 14 October 1969, see entire document	27,28,31
A	US, A, 4,338,564 (MUNDSCHENK) 06 July 1982, see column 7 lines 50-68, column 8 lines 13-47.	23-37,53-58

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [10]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers .... because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers..........., because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [11]

This International Searching Authority found multiple inventions in this international application as follows:

I. Claims 1-4 and 19-22 drawn to a volumetric transfer system; Class 422, subclass 100.

II. Claims 5-6 and 9 drawn to a method of transferring a liquid; Class 436, subclass 180.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

   1-4, 19-37, 53-58, 70-73

3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☒ No protest accompanied the payment of additional search fees.

International Application No.
PCT/US86/01350

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category*	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No [18]
VI	Continued III. Claims 7-8 drawn to a valve system; Class 137, subclass 624.11. IV. Claims 10-18 drawn to fluid handling process; Class 137, subclass 1. V. Claims 23-36 and 70-73 drawn to a method of curve fitting; Class 364, subclass 555. VI. Claims 37-and 53-58 drawn to a computer control blood cell counter; Class 422, subclass 67. VII. Claims 38-52 drawn to a calibrating system; Class 364, subclass 571. VIII. Claims 59-67 drawn to a counting system; Class 377, subclass 2. IX. Claims 68-69 drawn to an optical blood analyzer; Class 356, subclass 40.	